Clinical microbiological case: a Nicaraguan woman with skin lesions on the left elbow and foot

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A 75-year-old woman came to the hospital with malaise, mental obtundation and inflammatory lesions in the left elbow (Figures 1 and 2). She was rushed to hospital 3 h after arriving for vacation in Madrid from Nicaragua.

She had been suffering from type II diabetes mellitus for 15 years.

On admission, the patient was febrile (38.5 °C), tachycardic, tachypneic and hypotensive (blood pressure 90/60 mmHg). Blood cultures were drawn. Thoracic and left elbow radiographs were taken without significant findings. An arthrocentesis from the elbow drained 20 mL of synovial fluid. A lumbar puncture was performed. Analytic data were immediately collected (Table 1).

Three hours later, several skin lesions appeared over the patient's right foot, in the 2nd and 3rd toes, the dorsum and the heel. The evolution of these lesions after 48 h is shown in Figures 3–5.

Figure 1

QUESTIONS

Discuss the case, considering the following points:

1. What is the etiology of this entity?
2. What are its mechanisms of pathogenicity and the virulence factors associated with the microorganisms involved?
3. Is there any method for rapid and specific diagnosis of this infection?
4. Comment on what is the elective and adjuvant treatment of this disease.

Figure 2

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Figure 3

Figure 4

Figure 5

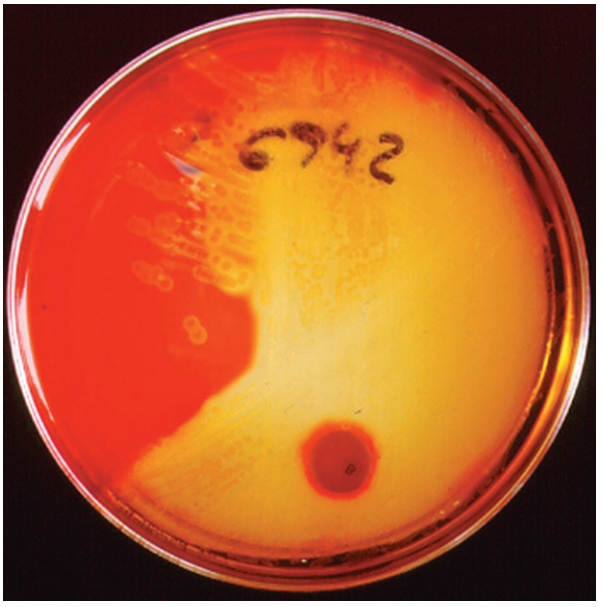

Figure 6

Table 1 Analytic data on admission

Blood	Synovial fluid	Cerebrospinal fluid
ESR 117 mm/1st hour	Yellowish color	Transparent
Hemoglobin 8.8 g/dL	–	Pressure 79 mmH_2O
Hematocrit 26.1%	Low viscosity	Proteins 30 mg/dL
Leukocytes 14 600/μL	Cells: 57 000/μL	Cells: 1–2/μL
Count 88% neutrophils	> 80% neutrophils	Monocytes
Glucose 190 mg/dL	Glucose 403 mg/dL	Glucose 101 mg/dL

CLINICAL OUTCOME

The Gram stain from the synovial fluid showed the presence of Gram-positive cocci arranged in chains. Rapid antigen detection for *Streptococcus pyogenes* (group A streptococci (GAS)) polysaccharide (PSC) in synovial fluid was also positive. Blood cultures and cultures from synovial fluid and skin biopsies grew GAS (Figure 6).

The patient was treated initially with intravenous penicillin (2 million IU every 4 h) but skin surgical debridement of the lesions was also necessary. Seven days later, intravenous clindamycin was added (600 mg every 6 h) to the treatment but the extension of the right foot lesions made amputation mandatory.

No other septic foci were detected and the patient was uneventfully discharged 20 days after admission.

DIAGNOSIS

Group A streptococcal gangrene.

DISCUSSION

1. The diagnosis of the skin and soft tissue infections is very broad. Skin, fascia and muscles are involved, and this also produces septic arthritis, bacteremia and sepsis [1–4]. Among the microorganisms able to produce such infections, we must include *Staphylococcus*, *Streptococcus* and Gram-positive anaerobic bacilli like *Clostridium* spp., although the Enterobacteriaceae, other anaerobic bacteria, *Pseudomonas* and some fungi can severely affect soft tissues, with systemic impairment [4,5]. In this case, the microbiological data confirm the diagnosis of *Streptococcus pyogenes* gangrene [6–10].

β-Hemolytic *Streptococcus* from group A of Lancefield (GAS), or *Streptococcus pyogenes*, is a Gram-positive bacterium that is arranged in chains and grows on blood agar cultures. It is catalase negative, susceptible to bacitracin and able to hydrolyze pirrolydonil betanaphthylamide (PYR). In blood agar cultures, the colonies produce an area of complete hemolysis (β) caused by the production of two hemolysins (streptolysins S and O) [11]. Their wall is formed by a PSC characteristic of group A and some structural proteins (proteins M, T and R). On the basis of typing M protein, GAS can be differentiated into more than 70 different serotypes. This protein induces antibodies which react with the cardiac tissue and are responsible for the pathogenesis of rheumatic fever [12]. Most of the strains of GAS responsible for invasive diseases are of the serotypes M1 and M3, although clusters of serious infections (shock, multiple organ failure) with other serotypes, M10, M12, M28 and M38, have been reported [13–15].

2. GAS frequently colonizes the human mucous membranes, particularly those of the upper respiratory tract (tonsils, pharynx), the gastrointestinal tract, the vagina and wet and warm skin folds [13,16,17].

The main virulence factors in this microorganism are: peptidoglycan *and* lipoteicoic acid, M protein, hemolysins (S and O streptolysins), enzymes (hyaluronidase, adenase and streptoquinase) and toxins [14,15,18–23].

3. Microbiological diagnosis [1,3,13]. The elements of an early diagnosis for such infections are: (a) direct sampling staining (skin biopsies, tissues, fascia, muscle, purulent exudate or arthrocentesis fluid) with traditional methods—Gram, acridine orange—and special histopathologic stains, such as Brown–Hopps Gram, Brown–Brenn Gram, Giemsa, Gomori; (b) rapid detection of capsular and protein antigens in skin and/or tissues—commercial kits for specific antigen are already available, with sensitivity between 60% and 91% and specificity between 85% and 98% [24]; (c) culture—in 18 h, we can observe the growth of typical β-hemolytic colonies in cultures on blood agar; (d) molecular techniques for bacterial detection of genome—these are not available in most laboratories.

4. For the treatment of non-severe infections, intravenous penicillin G 1–2 million U every 4 h is an adequate option [25,26]. In severe and invasive infections, although susceptible in vitro, the in vivo susceptibility of GAS is diminished. This type of 'resistance' may be caused by several factors, including the so-called 'Eagle' effect [27], limited postantibiotic effect, short duration of action of penicillin, in situ production of β-lactamases by other microorganisms (saprophytes) and the phenomenon of tolerance [28–30].

At the present time, combined treatment with clindamycin is preferred [28]. Its effectiveness is based on the following: (a) it is not affected by the size of the inoculum or the state of bacterial growth; (b) it is a powerful inhibitor of bacterial toxin synthesis; (c) it facilitates phagocytosis when inhibiting the synthesis of M protein; (d) it has a prolonged postantibiotic effect; and (e) it inhibits the synthesis of TNF induced by polysaccharide (PSC) in the monocytes.

The neutralization of circulating toxins by means of hyperimmune immunoglobulins is desirable, although its use has achieved clinical success only in cases of GAS invasive infections [31]. The dose and suitable duration of therapy are still not standardized. In this case, we used intravenous immunoglobulin at doses of 150 mg/kg per day for 10 days.

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